

FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>		ATTY. DOCKET NO. 0623.1090001/EKS/BJD	APPLICATION NO. 09/877,244
		APPLICANT STADDON et al.	RECEIVED
		FILING DATE June 11, 2001	GROUP 1645 1647
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
BL	AA1	5,155,031	10/13/92	Posner et al.	435	184	06/07/90
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
BL	AL1	WO 91/04745	04/18/1991	WIPO			Yes No
	AM1	JP 4-13631	01/17/1992	Japan			Abstract Yes No
	AN1	WO 95/13820	05/26/1995	WIPO			Yes No
	AO1	WO 96/16170	05/30/1996	WIPO			Yes No
↓	AP1	WO 98/14186	04/09/1998	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

BL	AR	1	Aberle, H., et al., "Cadherin-Catenin Complex: Protein Interactions and Their Implications for Cadherin Function," <i>J. Cell. Biochem.</i> 61:514-523, Wiley-Liss, Inc. (1996).
BL	AS	1	Anderson, J.M., et al., "The structure and regulation of tight junctions," <i>Curr. Opin. Cell Biol.</i> 5(5):772-778, Current Biology Ltd. (1993).
BL	AT	1	Balda, M.S., et al., "Assembly of the Tight Junction: The Role of Diacylglycerol," <i>J. Cell Biol.</i> 123(2):293-302, The Rockefeller University Press (1993).

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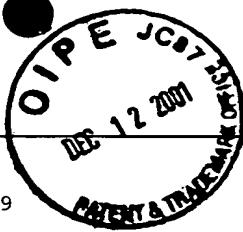
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	2	Behrens, J., et al., "Loss of Epithelial Differentiation and Gain of Invasiveness Correlates with Tyrosine Phosphorylation of the E-Cadherin/β-Catenin Complex in Cells Transformed with a Temperature-sensitive v-SRC Gene," <i>J. Cell Biol.</i> 120(3):757-766, The Rockefeller University Press (1993).
<i>BL</i>	AS	2	Breier, G., et al., "Angiogenesis in Embryos and Ischemic Diseases," <i>Thromb. Haemost.</i> 78:678-683, F.K. Schattauer Verlagsgesellschaft (July 1997).
<i>BL</i>	AT	2	Citi, S., "Protein Kinase Inhibitors Prevent Junction Dissociation Induced by Low Extracellular Calcium in MDCK Epithelial Cells," <i>J. Cell Biol.</i> 117:169-178, The Rockefeller University Press (1992).

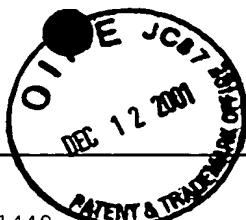
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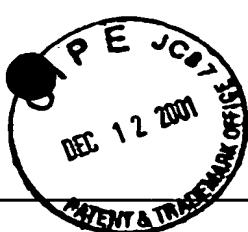
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<i>BL</i>	AR	3	Citi, S., et al., "The role of phosphorylation in the assembly and disassembly of epithelial junctions," Molec. Biol. Cell 3(Suppl.):218a, Abstract No. 1262, The American Society for Cell Biology (1992).
<i>BL</i>	AS	3	Collares-Buzato, C.B., et al., "Junctional uvomorulin/E-cadherin and phosphotyrosine-modified protein content are correlated with paracellular permeability in Madin-Darby canine kidney (MDCK) epithelia," Histochemistry 101:185-194, Springer-Verlag (1994).
<i>BL</i>	AT	3	Crow, D.S., et al., "Phosphorylation of connexin43 in cells containing mutant src oncogenes," Oncogene 7:999-1003, Nature Publishing Group (1992).

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<i>BL</i>	AR	4	Daniel, J.M., and Reynolds, A.B., "Tyrosine phosphorylation and cadherin/catenin function," <i>BioEssays</i> 19:883-891, The Company of Biologists Limited (October 1997).
<i>BL</i>	AS	4	Downing, J.R., and Reynolds, A.B., "PDGF, CSF-1, and EGF induce tyrosine phosphorylation of p120, a pp60 ^{src} transformation-associated substrate," <i>Oncogene</i> 6:607-613, Nature Publishing Group (1991).
<i>BL</i>	AT	4	Durieu-Trautmann, O., et al., "Nitric Oxide and Endothelin Secretion by Brain Microvessel Endothelial Cells: Regulation by Cyclic Nucleotides," <i>J. Cell. Physiol.</i> 155:104-111, Wiley-Liss, Inc. (1993).

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<i>BL</i>	AR	5	Fantus, I.G., et al., "Pervanadate [Peroxide(s)of Vanadate] Mimics Insulin Action in Rat Adipocytes via Activation of the Insulin Receptor Tyrosine Kinase," <i>Biochemistry</i> 28:8864-8871, American Chemical Society (1989).
<i>BL</i>	AS	5	Ferrara, N., and Davis-Smyth, T., "The Biology of Vascular Endothelial Growth Factor," <i>Endocrine Rev.</i> 18:4-25, The Endocrine Society (February 1997).
<i>BL</i>	AT	5	Filson, A.J., et al., "Tyrosine Phosphorylation of a Gap Junction Protein Correlates with Inhibition of Cell-to-Cell Communication," <i>Cell Growth Differ.</i> 1:661-668, American Association for Cancer Research (1990).

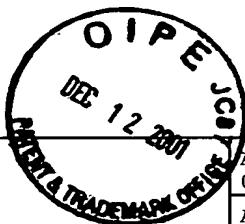
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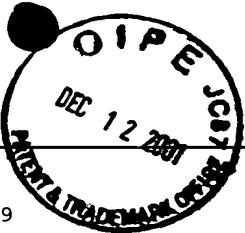
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<i>BL</i>	AR	6	Fong, T.A.T., et al., "SU5416 Is a Potent and Selective Inhibitor of the Vascular Endothelial Growth Factor Receptor (Flk-1/KDR) That Inhibits Tyrosine Kinase Catalysis, Tumor Vascularization, and Growth of Multiple Tumor Types," <i>Cancer Res.</i> 59:99-106, The American Association for Cancer Research (1999).
<i>BL</i>	AS	6	Galaktionov, K., and Beach, D., "Specific Activation of cdc25 Tyrosine Phosphatases by B-Type Cyclins: Evidence for Multiple Roles of Mitotic Cyclins," <i>Cell</i> 67:1181-1194, Cell Press (1991).
<i>BL</i>	AT	6	Garcia-Morales, P., et al., "Tyrosine phosphorylation in T cells is regulated by phosphatase activity: Studies with phenylarsine oxide," <i>Proc. Natl. Acad. Sci. USA</i> 87:9255-9259, The National Academy of Sciences (1990).

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	AL						Yes No
	AM						Yes No
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<i>BL</i>	AR	7	Gumbiner, B., and Simons, K., "A Functional Assay for Proteins Involved in Establishing an Epithelial Occluding Barrier: Identification of a Uvomorulin-like Polypeptide," <i>J. Cell Biol.</i> 102:457-468, The Rockefeller University Press (1986).
<i>BL</i>	AS	7	Gumbiner, B., et al., "The Role of the Cell Adhesion Molecule Uvomorulin in the Formation and Maintenance of the Epithelial Junctional Complex," <i>J. Cell Biol.</i> 107:1575-1587, The Rockefeller University Press (1988).
<i>BL</i>	AT	7	Gumbiner, B.M., "Cell Adhesion: The Molecular Basis of Tissue Architecture and Morphogenesis," <i>Cell</i> 84:345-357, Cell Press (1996).

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M	AR	8	Hamaguchi, M., et al., "p60 ^{v-src} causes tyrosine phosphorylation and inactivation of the N-Cadherin-catenin cell adhesion system," <i>EMBO J.</i> 12(1):307-314, Oxford University Press (1993).
M	AS	8	Hedrick, L., et al., "Cell adhesion molecules as tumour suppressors," <i>Trends Cell Biol.</i> 3(2):36-39, Elsevier Science Ltd. (1993).
M	AT	8	Heffetz, D., et al., "The Insulinomimetic Agents H ₂ O ₂ and Vanadate Stimulate Protein Tyrosine Phosphorylation in Intact Cells," <i>J. Biol. Chem.</i> 265:2896-2902, The American Society for Biochemistry and Molecular Biology, Inc. (1990).

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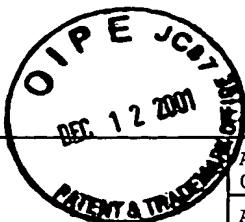
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<i>PL</i>	AR	9	Herrenknecht, K., et al., "Endothelial Cadherins And The Regulation Of Tight Junction Permeability," Abstract (distributed at meeting) from British Society for Immunology Spring Meeting 1994, University of Southampton, United Kingdom, March 23-25, 1994.
<i>PL</i>	AS	9	Izumi, T., et al., "Periodic Changes in Phosphorylation of the Xenopus cdc25 Phosphatase Regulate Its Activity," Mol. Biol. Cell 3:927-939, American Society for Cell Biology (1992).
<i>PL</i>	AT	9	John, V., et al., "The effect of cyclic AMP-dependent protein kinase inhibitors on electrical resistance in the cell culture model for the blood-brain barrier," Pharm. Pharmacol. Lett. 3:190-193, Springer-Verlag (1994).

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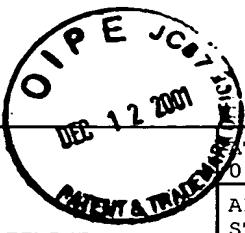
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<i>BL</i>	AR	<u>10</u>	Jones, A., and Harris, A.L., "New Developments in Angiogenesis: A Major Mechanism for Tumor Growth and Target for Therapy," <i>Cancer J.</i> 4:209-217, <i>Scientific American</i> (July-August 1998).
<i>BL</i>	AS	<u>10</u>	Kanner, S.B., et al., "Tyrosine Phosphorylation of a 120-Kilodalton pp60 ^{cc} Substrate upon Epidermal Growth Factor and Platelet-Derived Growth Factor Receptor Stimulation and in Polyomavirus Middle-T-Antigen-Transformed Cells," <i>Mol. Cell. Biol.</i> 11:713-720, <i>American Society for Microbiology</i> (1991).
<i>BL</i>	AT	<u>10</u>	Kurihara, H., et al., "Increased Tyrosine Phosphorylation Accompanies Modification of Tight Junctions Between Foot Processes of Glomerular Epithelial Cells (GEC)," <i>Mol. Biol. Cell</i> 3(Suppl.):218a, Abstract No. 1263, <i>American Society for Cell Biology</i> (1992).

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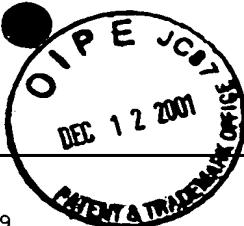
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<i>BL</i>	AR	<u>11</u>	Kurihara, H., et al., "Localization and Dynamics of Tight Junction Protein, ZO-1 in Rat Glomerular Epithelial Cells," <i>Cell Struct. Funct.</i> 17(6):493, Abstract No. 1D-1615, Japan Society of Cell Biology (1992).
<i>BL</i>	AS	<u>11</u>	Langelier, E.G., and van Hinsbergh, V.W.M., "Norepinephrine and iloprost improve barrier function of human endothelial cell monolayers: role of cAMP," <i>Am. J. Physiol.</i> 260:c1052-c1059, American Physiological Society (1991).
<i>BL</i>	AT	<u>11</u>	Levenson, R.M., and Blackshear, P.J., "Insulin-stimulated Protein Tyrosine Phosphorylation in Intact Cells Evaluated by Giant Two-dimensional Gel Electrophoresis," <i>J. Biol. Chem.</i> 264:19984-19993, The American Society for Biochemistry and Molecular Biology (1989).

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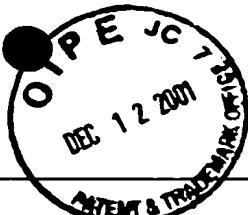
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<i>BL</i>	AR	<u>12</u>	Liebow, C., et al., "Somatostatin analogues inhibit growth of pancreatic cancer by stimulating tyrosine phosphatase," Proc. Natl. Acad. Sci. USA 86:2003-2007, The National Academy of Sciences (1989).
<i>BL</i>	AS	<u>12</u>	Linder, M.E., and Burr, J.G., "Nonmyristoylated p60 ^{v-src} fails to phosphorylate proteins of 115-120 kDa in chicken embryo fibroblasts," Proc. Natl. Acad. Sci. USA 85:2608-2612, The National Academy of Sciences (1988).
<i>BL</i>	AT	<u>12</u>	Lum, H., and Malik, A.B., "Mechanisms of increased endothelial permeability," Can. J. Physiol. Pharmacol. 74:787-800, NRC Canada (1996).

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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>		ATTY. DOCKET NO. 0623.1090001/EKS/BJD	APPLICATION NO. 09/877,244
		APPLICANT STADDON et al.	
		FILING DATE June 11, 2001	GROUP 16461647

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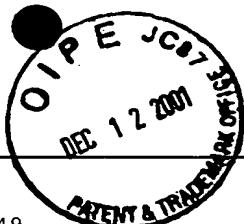
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	AL						Yes No
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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	<u>13</u>	Madara, J.L., "Tight Junction Dynamics: Is Paracellular Transport Regulated?," Cell 53:497-498, Cell Press (1988).
<i>BL</i>	AS	<u>13</u>	Martinez-Palomo, A., et al., "Experimental Modulation of Occluding Junctions in a Cultured Transporting Epithelium," J. Cell Biol. 87:736-745, The Rockefeller University Press (1980).
<i>BL</i>	AT	<u>13</u>	Matsuyoshi, N., et al., "Cadherin-Mediated Cell-Cell Adhesion Is Perturbed by v-src Tyrosine Phosphorylation in Metastatic Fibroblasts," J. Cell Biol. 118:703-714, The Rockefeller University Press (1992).

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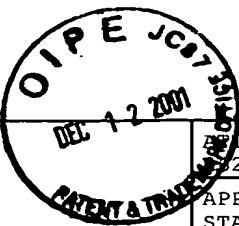
<i>BL</i>	AR	<u>14</u>	Morgan, L., et al., "Molecular Control of Blood Brain Barrier Permeability," Abstract (distributed at meeting) from 8th International Workshop on in Vitro Toxicology, Zurich, Switzerland, September 20-23, 1994.
<i>BL</i>	AS	<u>14</u>	Mullin, J.M., et al., "Modulation of tumor necrosis factor-induced increase in renal (LLC-PK ₁) transepithelial permeability," Am. J. Physiol. 263:F915-F924, American Physiological Society (1992).
<i>BL</i>	AT	<u>14</u>	Musil, L.S., et al., "Differential Phosphorylation of the Gap Junction Protein Connexin43 in Junctional Communication-competent and -deficient Cell Lines," J. Cell Biol. 111:2077-2088, The Rockefeller University Press (1990).

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<u>INFORMATION DISCLOSURE STATEMENT</u>		APPLICANT STADDON et al.	
		FILING DATE June 11, 2001	GROUP 1645 1647

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	AO						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BR</i>	AR	<u>15</u>	Neufeld, G., et al., "Similarities and differences between the vascular endothelial growth factor (VEGF) splice variants," <i>Cancer Metastasis Rev.</i> 15:153-158, Kluwer Academic Publishers (1996).
<i>BR</i>	AS	<u>15</u>	Ojakian, G.K., "Tumor Promoter-Induced Changes in the Permeability of Epithelial Cell Tight Junctions," <i>Cell</i> 23:95-103, MIT (1981).
<i>BR</i>	AT	<u>15</u>	Ratcliffe, M.J., et al., "Dephosphorylation of the Cadherin-associated p100/p120 Proteins in Response to Activation of Protein Kinase C in Epithelial Cells," <i>J. Biol. Chem.</i> 272:31894-31901, The American Society for Biochemistry and Molecular Biology, Inc. (December 1997).

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		APPLICANT STADDON et al.		
		FILING DATE June 11, 2001	GROUP 1645-1647	

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>Br</i>	AR	<u>16</u>	Ratcliffe, M.J., et al., "Dephosphorylation of the catenins p120 and p100 in endothelial cells in response to inflammatory stimuli," <i>Biochem. J.</i> 338:471-478, Biochemical Society (1999).
<i>Br</i>	AS	<u>16</u>	Rubin, L.L., et al., "A Cell Culture Model of the Blood-Brain Barrier," <i>J. Cell Biol.</i> 115:1725-1735, The Rockefeller University Press (1991).
<i>Br</i>	AT	<u>16</u>	Rubin, L.L., "Endothelial cells: adhesion and tight junctions," <i>Curr. Opin. Cell Biol.</i> 4:830-833, Current Biology Ltd. (1992).

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	AL						Yes No
	AM						Yes No
	AN						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	17	Rubin, L.L., and Staddon, J.M., "Regulation Of Blood-Brain Barrier Permeability," Abstract (distributed at meeting) from XXXII International Union of Physiological Sciences (IUPS) Congress, Glasgow, UK, August 4-6, 1993.
<i>BL</i>	AS	17	Rubin, L.L., et al., "Tight Junctions And The Blood-Brain Barrier," Abstract (distributed at meeting) from Association pour la Recherche sur La Scleroze en Plaques (ARSEP), Paris, France, December 1-2, 1993.
<i>BL</i>	AT	17	Rubin, L.L., et al., "Signal Transduction And The Blood-Brain Barrier," Abstract (distributed at meeting) from 17th Annual Meeting of the European Neuroscience Association, Vienna, Austria, September 4-8, 1994.

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	AO						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	<u>18</u>	Rubin, L.L., et al., "Tight Junctions and the Blood-Brain Barrier," in: <i>Cell Culture in Pharmaceutical Research</i> , Fusenig, N.E., and Graf, H., eds., Berlin: Springer-Verlag, pp. 69-77 (1994).
<i>BL</i>	AS	<u>18</u>	Rubin, L.L., et al., "Signal Transduction in Brain Endothelial Cells," Paper (distributed at meeting) presented at INSERM Meeting No. 67, In Vitro Models for Drug Transport Across Epithelial and Endothelial Barriers, Le Vesinet, France, October 13-14, 1994.
<i>BL</i>	AT	<u>18</u>	Rutten, M.J., et al., "Electrical resistance and macromolecular permeability of brain endothelial monolayer cultures," <i>Brain Res.</i> 425:301-310, Elsevier Science (1987).

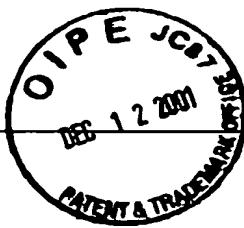
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	<u>19</u>	Soler, A.P., et al., "Tissue remodeling during tumor necrosis factor-induced apoptosis in LLC-PK ₁ renal epithelial cells," Am. J. Physiol. 270:F869-F879, American Physiological Society (1996).
<i>BL</i>	AS	<u>19</u>	Staddon, J.M., et al., "Tyrosine Phosphatase Inhibitors Increase Tight Junctional Permeability in Strain I MDCK Cells," Mol. Biol. Cell 4(Suppl.):103a, Abstract No. 599, American Society for Cell Biology (1993).
<i>BL</i>	AT	<u>19</u>	Staddon, J.M., et al., "Tyrosine Phosphorylation and Tight Junction Permeability. I," Abstract (distributed at meeting) from Autumn Meeting of the British Society for Cell Biology, University of Oxford, UK, September 18-21, 1994.

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	AN						Yes No
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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	<u>20</u>	Staddon, J.M., et al., "Evidence that tyrosine phosphorylation may increase tight junction permeability," <i>J. Cell Sci.</i> 108(2):609-619, The Company Of Biologists Ltd. (1995).
<i>BL</i>	AS	<u>20</u>	Staddon, J.M., et al., "p120, a p120-Related Protein (p100), and the Cadherin/Catenin Complex," <i>J. Cell Biol.</i> 130:369-381, The Rockefeller University Press (1995).
<i>BL</i>	AT	<u>20</u>	Stelzner, T.J., et al., "Role of Cyclic Adenosine Monophosphate in the Induction of Endothelial Barrier Properties," <i>J. Cell. Physiol.</i> 139:157-166, Alan R. Liss, Inc. (1989).

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	AO						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	21	Stevenson, B.R., et al., "Phosphorylation of the tight-junction protein ZO-1 in two strains of Madin-Darby canine kidney cells which differ in transepithelial resistance," <i>Biochem. J.</i> 263:597-599, Portland Press Ltd. (1989).
<i>BL</i>	AS	21	Sun, L., et al., "Synthesis and Biological Evaluations of 3-Substituted Indolin-2-ones: A Novel Class of Tyrosine Kinase Inhibitors That Exhibit Selectivity toward Particular Receptor Tyrosine Kinases," <i>J. Med. Chem.</i> 41:2588-2603, American Chemical Society (July 1998).
<i>BL</i>	AT	21	Swenson, K.I., et al., "Tyrosine phosphorylation of the gap junction protein connexin43 is required for the pp60 ^{-src} -induced inhibition of communication," <i>Cell Regul.</i> 1:989-1002, The American Society for Cell Biology (1990).

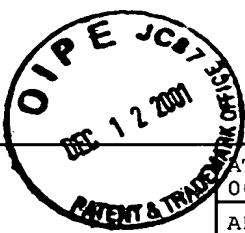
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		APPLICANT STADDON et al.	
		FILING DATE June 11, 2001	GROUP 1645 1647

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	22	Tsukita, S., et al., "Specific Proto-Oncogenic Tyrosine Kinases of src Family Are Enriched in Cell-to-Cell Adherens Junctions Where the Level of Tyrosine Phosphorylation Is Elevated," <i>J. Cell Biol.</i> 113:867-879, The Rockefeller University Press (1991).
<i>BL</i>	AS	22	Tsukita, S., et al., "Submembranous Junctional Plaque Proteins Include Potential Tumor Suppressor Molecules," <i>J. Cell Biol.</i> 123(5):1049-1053, The Rockefeller University Press (1993).
<i>BL</i>	AT	22	Vermeulen, S., et al., "Regulation of the Invasion Suppressor Function of the Cadherin/Catenin Complex," <i>Path. Pract.</i> 192:694-707, Gustav Fischer Verlag (1996).

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		APPLICANT STADDON et al.	
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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>BL</i>	AR	<u>23</u>	Volberg, T., et al., "The effect of tyrosine-specific protein phosphorylation on the assembly of adherens-type junctions," <i>EMBO J.</i> 11:1733-1742, Oxford University Press (1992).
<i>BL</i>	AS	<u>23</u>	Warren, S.L., and Nelson, W.J., "Nonmitogenic Morphoregulatory Action of pp60 ^{v-src} on Multicellular Epithelial Structures," <i>Mol. Cell. Biol.</i> 7:1326-1337, American Society for Microbiology (1987).
<i>BL</i>	AT	<u>23</u>	Wong, E.Y.M., et al., "Vascular endothelial growth factor stimulates desphosphorylation of the catenins p120 and p100 in endothelial cells," <i>Biochem. J.</i> 346:209-216, Biochemical Society (2000).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>Al</i>	AR	24	Uehara, Y., et al., "Irreversible Inhibition Of V-src Tyrosine Kinase Activity By Herbimycin A And Its Abrogation By Sulfhydryl Compounds," <i>Biochem. Biophys. Res. Commun.</i> 163:803-809, Academic Press, Inc. (1989).
<i>Bl</i>	AS	24	English-language abstract for Japanese patent document No. JP 4-13631 (Doc. Ref. No. AM1), Derwent WPI Accession No. 8942154.
	AT	24	Pending Non-Provisional United States Patent Application No. 09/848,353, Staddon et al., filed May 4, 2001.

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